REMARKS

Claims 1, 4, 7, 16, 17, 19, 20 and 21 have been amended. Claims 9, 10 and 12 have been canceled. The subject matter of Claims 9 and 10 have been incorporated into independent Claim 1. No new matter has been added by these amendments. Claims 3, 18, 22 and 23 were withdrawn. Thus, Claims 1, 2, 4-8, 11, 13-17, 19-21, and 30-31 are presented for further examination.

Objections

Claims 1, 2, 4-17, 19-21, 30 and 31 were objected to because Claim 1 recited "internally or externally," but it was not clear whether the Applicants were referring to the inside and outside of the enzyme or the particle or the droplet. Applicants have amended Claim 1 to specifically recite "oriented either towards the lumens of the particles or outwardly therefrom." In addition, for clarity, Claim 1 is amended, as suggested by the Examiner, to recite "...in which the enzyme molecules are immobilized... sites of the enzyme molecules being orientated..."

Claim 7 and dependent claims thereof were objected to because the claim recited the abbreviations "O phase," "W phase," "O/W emulsion" and "W/O emulsion." The terms are written out in full in amended Claims 7 and 8.

Claim 12 was objected to as not further limiting Claim 7. Applicants have canceled Claim 12, thereby objection the rejection moot.

Claim 10 was objected to for lacking commas. However, the Applicants have canceled Claim 10, thereby rendering the rejection moot.

Claim 16 was objected to for having semicolons instead of commas. Applicants have amended Claim 16 by substituting the semicolons with commas.

Claim 19 was objected to for reciting the acronym "HLB" without providing the full corresponding text. The claim is amended to recite "hydrophilic-lipophilic balance (HLB). In addition the Examiner suggested clear claim language, which the Applicants have incorporated in to Claim 19.

Indefiniteness

Claims 4, 17, 19 and 20 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

With regard to Claims 4 and 20, the term "modifier" was not defined in the specification and the Examiner found the term to be vague. Applicants have amended Claims 4 and 20 to further define that the modifier is selected from the group consisting of an amino acid, a protein and a long chain hydrocarbon aldehyde.

Claim 17 recited the term "mediator," but the term was not defined in the specification and its meaning was found to be unclear. The Examiner noted that an example of a reaction mediator is provided in the specification. Applicants have amended Claim 17 to recite "a reaction mediator."

In view of the foregoing remarks and corresponding claim amendments, the claims are in compliance with 35 U.S.C. § 112, second paragraph.

Anticipation

Claims 1, 2, 3 7-9, 11-17, 20 and 31 were rejected under 35 U.S.C. § 102(b) as anticipated by Goldberg et al. (U.S. Patent No. 4,671,954). Goldberg et al teaches cross-linking of a non-catalytic protein (albumin) where the cross-linking is performed from the outside inwards, and hence can be considered an encapsulation technique [pg 3, lines 6-14] using a catalytically inert protein as a co-polymer. In contrast, Claim 1 as amended recites a process for the formation of stabilized enzyme particles involving the use of a cross-linking agent and active site protectant during formation of the particles.

Goldberg et al also refers to the use of enzymes to be attached to the particles:

"It is a further object of the invention to provide hydrophilic microspheres which may be more readily modified by aqueous chemical methods to covalently attach proteins, enzymes, antibodies, immunostimulants, and other compounds to alter and improve microsphere properties." - Column 1 lines 63-68. In this case, the enzyme is not an integral part of the original particle, and hence the particle should rather be considered to be an immobilization support, similar to known supports/particles (with their inherent disadvantages compared to self-immobilized enzymes, such as a substantially reduced catalytic activity on a per volume basis, as well as significant enzyme inactivation occurring during the immobilization process).

Goldberg et al also refers to the use of enzymes to form particles: (Column 3 lines 36-44):

"It will be understood by those skilled in the art, having been exposed to the principles of the present invention, that any protein or polypeptide capable of forming a cross-linked

microsphere may be employed in the practice of the invention. Suitable such proteins or polypeptides include serum albumin, poly-L-lysine, poly-L-arginine, poly-L-histidine, polyglutamic acid, and any water soluble protein with functional amine groups such as enzymes, immunoglobulins, etc."

However, the Applicants found by experimental investigations that major enzyme deactivation takes place during the crosslinking process, so that the resultant product is not useful as a self-immobilized enzyme. This is ascribed to possible cross-linking and reaction of the cross-linker (e.g., glutaraldehyde) with molecular groups on the active sites of the enzyme, causing major loss in enzyme activity. Amended claim 1 provides for the use of a temporary active site protectant during the crosslinking process, which serves to preserve the activity of the enzyme and yield the resultant particle useful in biocatalysis applications. The use of an active site protectant is not disclosed nor even suggested, by Goldberg et al.

Obviousness

Goldberg et al. in view of Margolin et al.

Claims 1, 2, 4-9, 11-17, 20, 30 and 31 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Goldberg et al. (supra) in view of Margolin et al. (WO 01/62280).

As discussed above, Goldberg et al does not teach or even remotely suggest the use of a temporary active site protectant for any enzymes. Hence, amended Claim 1 is novel over Goldberg et al. The process of Claim 1 employs a technique in which enzyme activity is stabilized and immobilized without the requirement of a solid support, encapsulation or entrapment. In contrast, Goldberg et al. requires the incorporation of protein into fixed particles that are used for encapsulation of drugs, or possibly as a solid support for other proteins. The protein is used as a structural material, and enzyme activity is not considered at all. Accordingly, Goldberg et al makes no attempt to retain enzyme activity during processing. Its protein is thus merely a polypeptide polymer used as a component in an encapsulation material.

Regarding Margolin et al., it deals with the formation of cross-linked enzyme crystals (CLECs). In its process an enzyme is extensively purified and then crystallized. The crystal structure is subsequently made permanent by cross-linking the enzymes. This technique differs from the process of Claim 1 in at least the following aspects:

1. The process of Margolin et al. does not provide an emulsion.

2. The range of enzymes that can be treated in the manner of Margolin et al. is limited as not all enzymes can be crystallized.

3. The process of Margolin et al. does not allow for orientation of the enzyme, which the process of Claim 1 does.

4. As the enzyme needs to be a crystal, only one enzyme type can be included in the stabilized crystal particle (due to packing requirements); in contrast, the process of Claim 1 can incorporate multiple enzymes.

5. Crystals are tightly packed molecules, and this introduces an additional barrier to diffusion, which reduces the catalytic activity of the cross-linked enzyme crystal.

Most importantly, the combination of Goldberg et al. and Margolin et al. provide no reason to the skilled artisan to use of a temporary protectant as recited in amended Claim 1, either in the context of a lipase or in the context of enzymes in general. As such, the claims are not obvious in view of the cited references

Abe et al.

Claim 21 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Abe et al. (1997 J Fermentation and Bioengineering 83:555-560) in view of Gosen et al. (U.S. Patent No. 4,492,684). Abe et al. discloses a method of making an O/W emulsion of an enzyme, but does not disclose that the enzyme is cross-linked. Goosen et al. disclose that, when proteins in an O/W emulsion are cross-linked, the proteins are released from the emulsified droplets at a controlled rate, and the emulsion is more stable. Because Claim 21 now recites the limitations of amended Claim 1, and because neither Abe or Goosen teach or suggest the missing limitation of using a temporary protectant, Claim 21 is deemed non-obvious for the reasons articulated above with respect to Claim 1.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other

broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

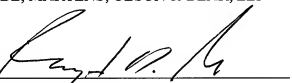
In view of Applicants' amendments to the Claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: September 28, 2009

By: 

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